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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,318	12/15/2003	Sunghwa Choe	11696-069002	6746

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,318	CHOE ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,9,11,13,15,17,19,21 and 23* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7,9,11,15,17,19,21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/15/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 6-7, 9, 11, 13, 15, 17, 19, 21, and 23 are pending.

2. Applicant's election with traverse of Group I, claims 6-7, 9, 11, 15, 17, 19, 21 and 23 in the reply filed on 2/28/2006 is acknowledged. The traversal is on the ground(s) that if a search and examination can be made without serious burden, the claims are to be examined on the merits (page 1 of Response, 2nd paragraph).

This is not found persuasive because while the search of the prior art for one group may overlap with that of another, they are not co-extensive of each other and thus would be a burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-5, 8, 10, 12, 14, 16, 18, 20, 22, and 24-35 have been canceled.

Claim 13 is withdrawn from consideration for being drawn to a non-elected invention.

3. Claims 6-7, 9, 11, 15, 17, 19, 21 and 23, including SEQ ID NO:22 are examined in the present office action.

Priority

4. The Office acknowledges Applicants' claim for domestic priority to application 09/775,879 filed 2/2/2001. Applicant is requested to amend the first paragraph to include the present status of said application.

Information Disclosure Statement

5. The information disclosure statement filed 12/15/2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication. In the instant application, the NCBI accession numbers do not include an author and date. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

6. Claim 6 is objected to for being drawn to a non-elected invention, i.e., "comprising at least 15 contiguous nucleotides".

Objection is made to the claims for not incorporating SEQ ID NO's when referring to nucleic acid or amino acid sequences. 37 CFR 1.821(d) requires the use of the assigned sequence identifier (e.g. SEQ I.D. NO: X) in all instances where the description or claims of a patent application discuss sequences.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 6-7, 11, 15, 17, 19, 21, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claim 6 is indefinite in the recitation "(b) a polynucleotide comprising a nucleotide sequence having at least 70% identity to the nucleotide sequence of (b)". The claim lacks a proper comparative basis.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 6-7, 11, 15, 17, 19, 21, and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated *dwf7* polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide comprises the nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or comprises a nucleotide sequence having at least 70% identity to itself, or a fragment or complements thereof; or wherein

said polynucleotide consists of the nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or the complement thereof, a recombinant vector comprising said polynucleotide, a host cell transformed with said vector, a transgenic plant or methods comprising said polynucleotide.

Given the indefiniteness of "(b) a polynucleotide comprising a nucleotide sequence having at least 70% identity to the nucleotide sequence of (b)" as discussed above, the Office interprets this to mean a polynucleotide comprising a nucleotide sequence having at least 70% identity to SEQ ID NO:22.

Applicants elected SEQ ID NO:22 which is the nucleic acid sequence encoding the HOMOLOG OF DWF7 (HDF7) protein from Arabidopsis, wherein said HDF7 is 80% identical in amino acid sequence with DWF7/STE1 (page 53, lines 20-25). Applicants disclose *dwf7* mutants having a dwarf phenotype, short robust stems, reduced fertility and dark-green, round and curled leaves (page 45, lines 12-13). The mutant plants also have a prolonged life span (page 45, line 19). Applicants disclose the DWF7 protein is a delta 7 sterol-C-5 desaturase (page 54, line 4). Applicants disclose the nucleic acid sequence and encoded protein of HDF7 in Figure 10 (page 3 of amended specification).

Applicants disclose in the Brief Description of the Drawings that Figures 10A-10F (SEQ ID NO:22) show the gene sequence of the *dwf7* homologue, *HWF7*. The coding sequence and corresponding amino acid sequence are shown in three segments (exons), occuring at positions 1506-1734, 2024-2329 and 2416-2720 of the figures. The 5' UTR is shown at positions 1-1505 and the 3' UTR occurs at positions 2721-2925. The Office contends that Applicants have not disclosed the complete coding sequence because results from a sequence search request of SEQ

ID NO:22 show the 5' untranslated region of SEQ ID NO:22 to align with a coding region of the Δ^7-sterol-C5-desaturase of Choe et al (1999, The Plant Cell 11(2):207-221, listed in IDS and NCBI accession number AF105034). Nucleotides 1-1366 of SEQ ID NO:22, which Applicants discloses as part of the 5' untranslated region, align with nucleotides 929-2294 of the Δ^7-sterol-C5-desaturase of Choe et al, wherein nucleotides 929-2294 are part of the coding region. In fact, within this region, the alignment exhibits 99% identity (see sequence search results). The same part of SEQ ID NO:22 also aligns with another cloned Δ^7-sterol-C5-desaturase of Husselstein et al (1999, Plant Mol. Biol. 39:891-906, listed in IDS and NCBI Accession number AF069468). Husselstein et al disclose that nucleotides 2029 to 2993 of their cloned sequence include the later half of the second exon and all of the third exon (See page 897, Figure 2) and this sequence aligns almost perfectly with nucleotides 1-964 of Applicants' SEQ ID NO:22 (see enclosed sequence search results).

The Applicants do not identify essential regions of HWF7 protein encoded by SEQ ID NO:22, nor do Applicants describe any polynucleotide sequences that have at least 70% identity to SEQ ID NO:22 that encode a functional HWF7 protein.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of

cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences encoding a HWF7 protein falling within the scope of the claimed genus of polynucleotides having at least 70% identity to SEQ ID NO:22. Applicants only describe a single sequence of SEQ ID NO:22. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the HWF7 protein, it remains unclear what features identify an Arabidopsis HWF7 protein. Since the genus of HWF7 proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

9. Claims 6-7, 11, 15, 17, 19, 21, and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists

a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated *dwf7* polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide comprises the nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or comprises a nucleotide sequence having at least 70% identity to itself, or a fragment or complements thereof; or wherein said polynucleotide consists of the nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or the complement thereof, a recombinant vector comprising said polynucleotide, a host cell transformed with said vector, a transgenic plant or method of producing a transgenic plant, method for altering the sterol composition of a plant relative to a wild-type plant comprising introducing said polynucleotide into a plant, or wherein the transgenic plant has less cholesterol or has increased sterol production relative to the wild-type plant.

Applicants elected SEQ ID NO:22 which is the nucleic acid sequence encoding the HOMOLOG OF DWF7 (HDF7) protein from Arabidopsis, wherein said HDF7 is 80% identical in amino acid sequence with DWF7/STE1 (page 53, lines 20-25). Applicants disclose *dwf7* mutants having a dwarf phenotype, short robust stems, reduced fertility and dark-green, round and curled leaves (page 45, lines 12-13). The mutant plants also have a prolonged life span

(page 45, line 19). Applicants disclose the DWF7 protein is a delta 7 sterol-C-5 desaturase (page 54, line 4).

Applicants have not reduced to practice their invention. The specification fails to provide guidance for one of skill in the art how to make and/or use the claimed invention. Applicants have not transformed a wild-type plant with any of the claimed sequences to produce a plant with an agronomically useful phenotype. Applicants have only taught that the isolated nucleic acid sequence of SEQ ID NO:22 encodes a homolog of the DWF7/STE1 gene. Applicants have not taught how one skilled in the art can use the claimed sequences to generate a plant with an agronomically useful phenotype without having to do additional undue experimentation in order to achieve the desired results. In addition, Applicants have not taught how one skilled in the art would use a plant transformed with any of the claimed sequences.

The state-of-the-art teaches transforming plants with a nucleic acid encoding a Δ^7-sterol-C5-desaturase produces unpredictable results. Husselstein et al (1999, Plant Mol. Biol. 39(5):891-906; listed in IDS) disclose Arabidopsis plants transformed with a nucleic acid encoding the STE1 protein produced plants that exhibited wild-type levels of Δ^7-sterols (page 902, Table 3). Husselstein et al state "allele dosage does not affect expression" (page 902, left column, 1st paragraph). Husselstein et al also state "Finally, transgenic *ste1-1* lines grown in the greenhouse displayed no dramatic morphological changes as compared to untransformed *ste1-1* or to wild-type Arabidopsis (page 902, 2nd full paragraph).

Hamada et al (1998, Plant Physiology 118:591-598; listed in IDS) teach that expressing heterologous desaturases in plants does not always give predictable results. Hamada et al overexpressed a tobacco microsomal α-3 fatty acid desaturase cDNA (NtFAD3) under the

control of a mosaic constitutive promoter that confers about 10-fold higher levels of constitutive expression than the CaMV 35S promoter. The results of overexpression in tobacco plants resulted in a 40% increase in alpha-linolenic acid in roots and only a 10% increase in leaves (abstract and page 593, right column, 1st paragraph of results). These results suggest that endogenous factors contribute to the observed result that cannot be predicted a priori.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that are 70% sequence identical to nucleotides 1506-2720 of SEQ ID NO:22 will encode a protein with the same activity as a protein encoded by SEQ ID NO:22. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

Re: claims 21 and 23 are drawn to a method for altering sterol composition in a plant, wherein the plant has either less cholesterol or the plant has increased sterol production. Applicants have not disclosed how transforming a plant with their invention will produce plants with either increased sterol or less cholesterol. It is unclear to the Office how the same method steps can produce opposite phenotypes.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:22 as probes or by designing primers to undisclosed regions of SEQ ID NO:22 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed produce a plant with an agronomically useful phenotype, a phenotype not disclosed by Applicant.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 6, 9, and 11 are rejected under 35 U.S.C. 102(a) as being anticipated by Choe et al (1999, The Plant Cell 11(2):207-221; listed in IDS).

The claims are drawn to an isolated *dwf7* polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide comprises complements of the

nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or comprises complements of a nucleotide sequence having at least 70% identity to itself; a recombinant vector comprising said polynucleotide, and a host cell transformed with said vector.

The Office interprets "complements" to mean any complement, which reads on any sequence comprising at least one base from Applicants' SEQ ID NO:22.

Choe et al teach a nucleic acid sequence exhibiting 46% sequence identity to Applicants' SEQ ID NO:22 (sequence search results included) and as discussed above, comprises a complement of any of the above recited claimed sequences. For purposes of molecular biology, the sequence would be in a vector, operably linked to a transcriptional control element and transformed into a host cell, and as such, Choe et al anticipate the claimed invention.

11. Claims 1, 9, 11, 15, 17, 19, 21, and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Husselstein et al (1999, Plant Mol. Biol. 39(5):891-906; listed in IDS).

The claims are drawn to an isolated *dwf7* polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide comprises complements of the nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or comprises complements of a nucleotide sequence having at least 70% identity to itself; a recombinant vector comprising said polynucleotide, a host cell transformed with said vector, a transgenic plant or method of producing a transgenic plant, method for altering the sterol composition of a plant relative to a wild-type plant comprising introducing said polynucleotide into a plant, or wherein the transgenic plant has less cholesterol or has increased sterol production relative to the wild-type plant.

The Office interprets "complements" to mean any complement, which reads on any sequence comprising at least one base from Applicants' SEQ ID NO:22.

Husselstein et al disclose a nucleotide sequence encoding a STE1 protein that has delta 7-sterol-C5(6)-desaturase activity and exhibits 32% sequence identity with Applicants' SEQ ID NO:22 (sequence search results included). Husselstein et al disclose a vector comprising said sequence operably linked to the 35S promoter and Arabidopsis plants transformed therewith (page 895, right column, see "Expression vector construction" and "Plant transformation"). Husselstein et al disclose that *ste1* mutant plants transformed with said vector restored reduced amounts of sterols to wild-type plant levels; increased the amount of sterols in the mutant plant (see for example page 902, Table 3). The Office contends that claims 21 and 23 are drawn to opposite products, i.e., less cholesterol and increased sterol production, respectively. But, because the recited method steps are identical, the Office contends that the disclosure of Husselstein et al reads on both claims, and as such, Husselstein et al anticipates the claimed invention.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 6, 9, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Gachotte et al (1996, The Plant Journal 9(3):391-398; listed in IDS).

The claims are drawn to an isolated *dwf7* polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide comprises complements of the nucleotide sequence depicted at positions 1506-2720 of Figures 10A-10F, or comprises complements of a nucleotide sequence having at least 70% identity to itself; a recombinant vector comprising said polynucleotide, and a host cell transformed with said vector.

The Office interprets "complements" to mean any complement, which reads on any sequence comprising at least one base from Applicants' SEQ ID NO:22.

Gachotte et al teach a nucleic acid sequence exhibiting 16% sequence identity to Applicants' SEQ ID NO:22 (sequence search results included), a vector comprising said nucleic acid sequence and yeast transformed therewith (pages 396-397, Experimental procedures), and as such, Gachotte et al anticipate the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claim 11 is rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The claim recites "A host cell comprising" which reads on a human being. Amending the claim to recite "An isolated host cell" will obviate the rejection.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
April 17, 2006

STUART F. BAUM, PH.D.
PATENT EXAMINER